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PATENT COOPERATION TREATY

FRIDAY, 16 JUL 2004

Rec'd PCT/PTO 15 FEB 2005

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Davies Collison Cave
Level 15
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MELBOURNE VIC 3000

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

EJH

	Date of mailing *day/month/year* 14 JUL 2004
Applicant's or agent's file reference 12315610/EJH/ar	**IMPORTANT NOTIFICATION**

International Application No.	International Filing Date	Priority Date
PCT/AU2003/001038	15 August 2003	15 August 2002

Applicant

THE CORPORATION OF THE TRUSTEES OF THE ORDER OF THE SISTERS OF MERCY IN QUEENSLAND et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	M. ONG Telephone No. (02) 6283 2491

PATENT COOPERATION TREATY

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 12315610/EJH/ar	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/001038**	International Filing Date *(day/month/year)* 15 August 2003	Priority Date *(day/month/year)* 15 August 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] A61K 39/395, A61P 37/06

Applicant

THE CORPORATION OF THE TRUSTEES OF THE ORDER OF THE SISTERS OF MERCY IN QUEENSLAND et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of **3** sheet(s).

3. This report contains indications relating to the following items:

I	[X]	Basis of the report
II	[ ]	Priority
III	[ ]	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	[ ]	Lack of unity of invention
V	[X]	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	[X]	Certain documents cited
VII	[ ]	Certain defects in the international application
VIII	[ ]	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
27 February 2004	2 July 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **M. ONG** Telephone No. (02) 6283 2491

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/AU2003/001038

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **1-45,** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages **46-48** , received on **21 June 2004** with the letter of **21 June 2004**
- [X] the drawings, pages **1-16** , as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-20**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1-20**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1-20**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1: WO 2001/078768
D2: WO 1999/024554
D3: WO 2002/080952
D4: WO 2003/012111
D5:KOPPI, T et al.

Novelty (N): Claims 1-20

The invention is directed to the modulation of the immune-activity in a subject cell or immuno-competent graft, by the administration of an antibody or antigen-binding fragment that couples, binds or otherwise associates with myeloid DC's and /or T cell's surface activation molecule. The interaction of the antibody with the cell surface activation molecule ie. CD83 molecule, would in turn prevent, inhibit or otherwise down-regulate one or more functional activities of said DC and/or T-cell, by inducing cell lysis.

The antibody comprises in the preferred embodiment a monoclonal antibody specific for CD83. The modulation of the immuno-activity of the cells is used as a method to down-regulate immuno-activity of bone marrow grafts in a subject and used where immuno-suppression is required, for example in graft versus host disease.

The closest prior art, D1, teaches one or more MHC-peptide complexes linked to an antibody specific for a cell surface marker of a professional antigen presenting cell for example, the cell surface marker of a dendritic cell or a T cell, eg. CD83, for the modulation of the immune response.

Claims 1-20 meet the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose an antibody or a monoclonal antibody per se, specific for CD83 for the purpose of modulating immuno-activity of a subject cell or an immuno-competent graft by inducing cell lysis.

Inventive Step (IS):Claims 1-20

Claims 1-20 meet the criteria set out in PCT Article33(3) with regard to the requirement of Inventive step because the prior art does not obviously suggest to a person skilled in the art the use of an antibody or a monoclonal antibody per se, specific for CD83 for the purpose of modulating immuno-activity of a subject cell or an immuno-competent graft by inducing cell lysis.

Industrial Applicability: Claims 1-20

Claims 1-20 have industrial applicability.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
P,X WO 2002/080952	17 October 2002	9 April 2002	9 April 2001
P,X WO 2003/012111	13 February 2003	25 July 2002	25 July 2001
P, X Koppi et al	27 May 2003		

With regard to the documents listed in Box VI under "certain documents cited", these are documents published prior to the international filing date but later than the priority date claimed but which would otherwise be considered to be of particular relevance.

Under the PCT, novelty is considered only in respect of documents published before the priority date. The relevance of a document published after the priority date is dependent upon national law. Such documents are excluded from consideration in preliminary examination, under the PCT Guidelines but have been included here for information.

This opinion has been based on the assumption that the claimed subject matter of the present application validly derives its priority claims.

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

CLAIMS

1. A method for modulating immuno-activity of a cell selected from a stimulator myeloid dendritic cell (DC) and a responder $CD4^+CD8^-$ T cell or $CD4^-CD8^+$ T cell said method comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which couples, binds or otherwise associates with CD83 and in turn prevents, inhibits or otherwise down-regulates one or more functional activities of said cell by inducing cell lysis .

2. The method of claim 1 wherein the antibody is a monoclonal antibody or a functional equivalent thereof.

3. The method of claim 1 wherein the cell is mammalian derived.

4. The method of claim 3 wherein the mammalian cell is a human cell.

5. The method of claim 2 wherein the functional equivalent is an antigen-binding derivative, fragment, homolog, analog or chemical equivalent of the antibody.

6. The method of claim 1 wherein lysis is caused by antibody-dependent cell-mediated cytotoxicity.

7. The method of claim 2 wherein the antibody in conjugated with a toxic component which induces or otherwise facilitates lysis of the APC and/or lymphocyte.

8. A method for modulating the immuno-activity of a myeloid DC and/or T cell, said method comprising contacting said DC and/or T cell with an effective amount of a monoclonal antibody specific for CD83 for a time and under conditions sufficient to prevent, inhibit or otherwise down-regulate one or more of antigen endocytosis, antigen processing and/or antigen presentation by said DC and activation of macrophages, stimulation of antibody production, and/or killing of target cells by ___

said T cell.

9. A method for modulating an immune response in a subject, said method comprising administering to said subject an effective amount of an antibody which couples, binds or otherwise associates with a myeloid DC's and/or T cell's surface activation molecule for a time and under conditions sufficient to induce cell lysis of said DC and/or T cell.

10. A method for down-regulating the immuno-activity of an immuno-competent graft, said method comprising administering to said subject an effective amount of an antibody which couples, binds or otherwise associates with a myeloid DC's and/or a T cell's CD83 molecule, for a time and under conditions sufficient to induce cell lysis of said DC and/or a T cell.

11. A method for down-regulating the immuno-activity of a bone marrow graft in a subject, said method comprising administering to said subject an effective amount of monoclonal antibody against CD83, for a time and under conditions sufficient to prevent, inhibit or otherwise down-regulate one or more functional activities of a DC and/or T-cell by inducing cell lysis.

12. A method for the prophylactic and/or therapeutic treatment of a condition characterized by the aberrant, unwanted or otherwise inappropriate immuno-activity of an immuno-competent graft, said method comprising contacting said graft with an effective amount of an antibody or a derivative, homolog, analog, chemical equivalent or mimetic thereof, which couples, binds or otherwise associates with a myeloid DC's and/or a T cell's surface activation CD83 molecule, for a time and under conditions sufficient to prevent, inhibit or otherwise down-regulate the immuno-activity of said DC and/or T cell by inducing cell lysis.

13. The method of claim 17 wherein the immuno-competent graft comprises allogenic bone marrow cells.

14. The method of claim 12 wherein the lymphocyte is a $CD4^+$ $CD8^-$ or $CD4^-$ $CD8^+$ T cell.

15. A method for the prophylactic and/or therapeutic treatment of a condition characterized by the aberrant, unwanted or otherwise inappropriate immuno-activity of an immuno-competent graft in a subject, said method comprising contacting said graft with an effective amount of an antibody or a derivative, homolog, analog, chemical equivalent or mimetic thereof, which couples, binds or otherwise associates with a myeloid DC's and/or a T cell's CD83 molecule derived from said graft, for a time and under conditions sufficient to prevent, inhibit or otherwise down-regulate the said inappropriate immuno-activity of said graft by inducing cell lysis.

16. The method of claim 15 wherein the subject is a mammal.

17. The method of claim 16 wherein the mammal is a human.

18. The method of claim 15 wherein the condition is graft *versus* host disease.

19. The method of claim 15 wherein the graft is an allergenic bone marrow graft, spleen cell graft or stem cell graft.

20. A method for the prophylactic and/or therapeutic treatment of a condition characterized by an aberrant, unwanted or otherwise inappropriate immune response in a subject, said method comprising administering to said subject an effective amount of an antibody or antigen-binding fragment thereof which couples, binds or otherwise associates with CD83 on the surface of a myeloid DC's and/or a $CD4^+CD8^-$ T cell or $CD4^-CD8^+$ T cell, for a time and under conditions sufficient to prevent, inhibit or otherwise down-regulate the immuno-activity of said DC and/or T cell by inducing cell lysis.